

REMARKS

Applicants respectfully request reconsideration and reexamination of the present application in light of the amendments and the remarks below.

Claims 1-30 are pending in this application. Applicants elected Group I, drawn to compounds of Formula (I) wherein Ar is phenyl, pharmaceutical compositions, methods of preparation, and methods of use (Paper No. Response to Restriction mailed July 8, 2004).

Claims 7, 16, 26, 27, 29, and 30 have been cancelled. Claims 1 and 4-6 have been amended by canceling the non-elected subject matter (i.e., where Ar is not phenyl). These claim amendments are made to clarify the subject matter therein. Therefore, these amendments are submitted in order to place the claims in condition for allowance, and do not disclaim any subject matter to which the Applicants are entitled.

Rejection Under 35 U.S.C. §§ 101

The Examiner rejected claims 7 and 16 under 35 U.S.C. § 101 as reach-through claims, because the claimed invention is not supported by either a specific and substantial asserted utility or well-established utility (Paper No. 20040819, page 4).

Claims 7 and 16 have been cancelled. Thus, Applicants respectfully requested reconsideration and withdrawal of the present rejection.

Rejection Under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 7 and 16 under 35 U.S.C. § 112, first paragraph, as reach-through claims (Paper No. 20040819, page 3). The claims are directed to a method of treating a beta-3 adrenergic receptor-mediated condition, yet these claims do not meet requirements for “how to use” under 35 U.S.C. 112, first paragraph, and 35 U.S.C. 101.

Claims 7 and 16 have been cancelled. Thus, Applicants respectfully requested reconsideration and withdrawal of the present rejection.

Claim Objections

The Examiner objected to claims 26, 27, 29, and 30 as being substantial duplicates of claims 25 and 28 (Paper No. 20040819, pages 4-5).

Claims 26, 27, 29, and 30 have been cancelled. Thus, Applicants respectfully requested reconsideration and withdrawal of the present objection.

Allowable Subject Matter

The Examiner stated that claims 1-6 would appear to be allowable over the prior art if non-elected subject matter is cancelled from the claims (Paper No. 20040819, page 5).

Claims 1-6 have been amended to recite Ar is phenyl. The non-elected subject matter has been cancelled.

The Examiner also stated that claims 8-15, 17-25, and 28 are currently free from the prior art (Paper No. 20040819, page 5).

CONCLUSION

For the foregoing reasons, Applicants submit that the claims are in condition for allowance and Applicants respectfully request reexamination of the present application, reconsideration and withdrawal of the present rejections and objections, and entry of the amendments. Should there be any further matter requiring consideration, Examiner Coppin is invited to contact the undersigned counsel.

If there are any further fees due in connection with the filing of the present reply, please charge the fees to undersigned's Deposit Account No. 13-3372. If a fee is required for an extension of time not accounted for, such an extension is requested and the fee should also be charged to undersigned's deposit account.

Respectfully submitted,



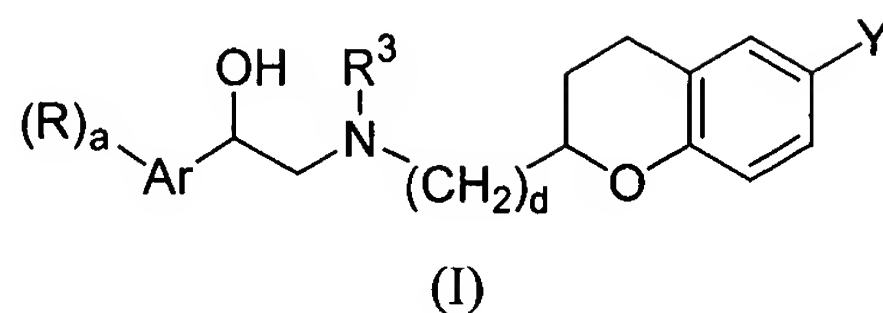
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Amendment to Claims (Attorney Docket No. 5062C1)

1. (Currently amended) A compound of Formula I



wherein,

R is independently

- hydroxy,
- oxo,
- halo,
- cyano,
- nitro,
- C₁-C₁₀ alkyl,
- C₁-C₁₀ haloalkyl,
- CF₃,
- NR¹R¹,
- SR¹,
- OR¹,
- SO₂R²,
- OCOR²,
- NR¹COR²,
- COR²,
- NR¹SO₂R²,
- phenyl, or
- a 5- or 6-membered heterocycle with from 1 to 4 heteroatoms selected from O, S, and N;

each cyclic moiety being optionally substituted with

- hydroxy,
- R¹,
- halo,

- cyano,
- NR^1R^1 ,
- SR^1 ,
- CF_3 ,
- OR^1 ,
- $\text{C}_3\text{-C}_8$ cycloalkyl,
- NR^1COR^2 ,
- COR^2 ,
- SO_2R^2 ,
- OCOR^2 ,
- $\text{NR}^1\text{SO}_2\text{R}^2$,
- $\text{C}_1\text{-C}_{10}$ alkyl, or
- $\text{C}_1\text{-C}_{10}$ alkoxy;

R^1 is

- hydrogen,
 - $(\text{CH}_2)_d\text{-O-(CH}_2)_d\text{R}^5$ where each d is selected independently, or
 - $\text{C}_1\text{-C}_{10}$ alkyl optionally substituted with 1 to 4 substituents each independently selected from
 - hydroxy,
 - halo,
 - $\text{CO}_2\text{C}_1\text{-C}_4\text{-alkyl}$,
 - CO_2H ,
 - $\text{C}_1\text{-C}_{10}$ alkoxy,
 - $\text{S(O)}_b\text{C}_1\text{-C}_{10}$ alkyl,
 - $\text{S(O)}_b\text{-phenyl}$ optionally substituted with halo, $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_1\text{-C}_4$ alkoxy, $\text{SO}_2\text{-C}_1\text{-C}_4\text{alkyl}$, or $\text{CO}_2\text{ C}_1\text{-C}_4\text{alkyl}$; or
 - phenyl optionally substituted with $\text{CO}_2\text{C}_1\text{-C}_4\text{-alkyl}$, CO_2H , halo, or $\text{C}_1\text{-C}_{10}$ alkyl;
- or
- $\text{C}_3\text{-C}_8$ cycloalkyl, phenyl, or naphthyl, each optionally substituted with 1 to 4 substituents each independently selected from halo, nitro, oxo, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_1\text{-C}_{10}$ alkoxy, $\text{C}_1\text{-C}_{10}$ alkylthio, $\text{CO}_2\text{C}_1\text{-C}_4\text{-alkyl}$, and CO_2H ,

and

when two R^1 groups are attached to N as NR^1R^1 , these R^1 groups may form together with the nitrogen to which they are attached, a heterocyclic ring containing 4 to 7 C atoms, 1 to 2 N atoms, and 0 to 1 O or S atoms;

R^2 is

- R^1 ,
 - OR^1 ,
 - NR^1R^1 ,
 - $NHS(O)_b$ phenyl optionally substituted with C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo or nitro;
 - $NHS(O)_b$ naphthyl,
 - $NHS(O)_bC_1$ - C_{10} alkyl optionally substituted with fluoro up to the perfluoro level,
- or
- a 5- or 6-membered heterocycle with one or more heteroatoms selected from O, S, and N, said heterocyclic moiety being optionally substituted with R^1 ;

R^3 is hydrogen, C_1 - C_{10} alkyl, or COR^2 ;

R^4 is hydrogen, C_1 - C_{10} alkyl, C_1 - C_{10} alkyl-phenyl, or C_1 - C_{10} alkyl-pyridyl;

R^5 is hydrogen or $COOH$;

R^6 is

- hydrogen,
- C_1 - C_{10} alkyl optionally substituted with 1 to 4 substituents each independently selected from halo, phenyl, or phenyl- COR^2 , or
- C_1 - C_{10} alkyl- $S(O)_bC_1$ - C_{10} alkyl optionally substituted with COR^2 or C_3 - C_8 cycloalkyl;

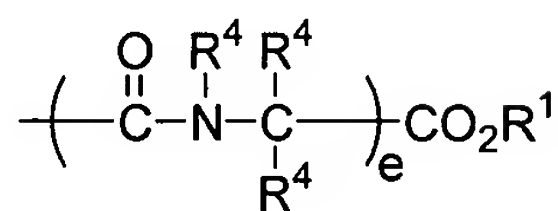
Ar is

- ~~phenyl optionally fused to a 5- or 6-membered heterocycle containing one or more heteroatoms each independently selected from O, S, and N, said bicyclic moiety being optionally fused to a phenyl, or~~
- ~~a 5- or 6-membered heterocycle containing one or more heteroatoms each independently selected from N, S, and O, optionally fused to phenyl;~~

Y is

- halo,
- NO_2 ,

- R⁶,
- SR¹,
- S(O)_b-phenyl-CO₂R¹,
-



where, when the two R⁴ groups attached to the same C are both alkyl, they optionally may be joined so that, when taken together with the C to which they are attached, they form a spiro ring of 3, 5, or 6 C atoms, or where the R⁴ attached to N and one R⁴ attached to the adjacent C are both alkyl, they optionally may be joined so that, taken together with the atoms to which they are attached, they form a 5- or 6-membered heterocyclic ring;

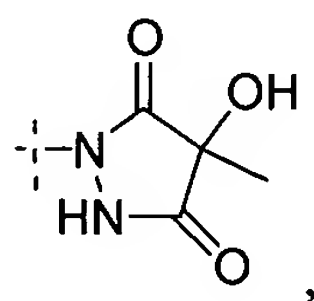
with the proviso that when e is 1, at least one R⁴ group must be C₁-C₁₀ alkyl-phenyl or C₁-C₁₀ alkyl-pyridyl, or two R⁴ groups must form one of said spiro or heterocyclic ring moieties;

- phenyl optionally fused to one or two phenyl rings, or to a 5- or 6-membered heterocycle containing one or more heteroatoms each independently selected from N, S, and O, or
 - a 5- or 6-membered heterocycle containing one or more heteroatoms each independently selected from N, S and O, optionally fused to a phenyl ring,
- each cyclic moiety being optionally substituted with one or more substituents independently selected from

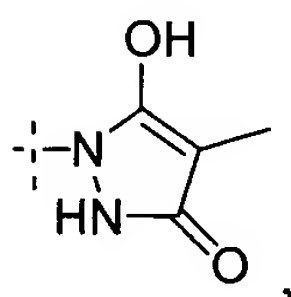
- COR²,
- CONR¹S(O)₂R⁹,
- COCH₂SO₂-thiazolyl optionally substituted with alkyl or amino,
- halo,
- NO₂,
- OR¹,
- R¹,
- SR¹,
- O-C₁-C₆-alkyl substituted by C₃-C₆-cycloalkyl,

- O-phenyl optionally substituted by SO_2CH_3 ,
- SO_2NH_2 ,
- $\text{SO}_2\text{NR}^1\text{R}^7$,
- NR^1R^1 ,
- $\text{NR}^1\text{COC}_1\text{-C}_6\text{alkyl}$,

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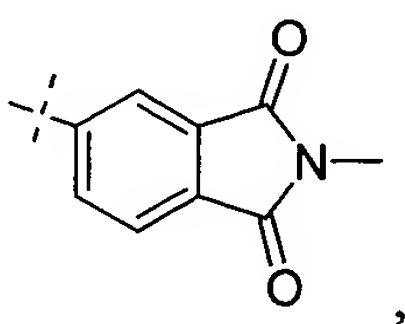


- $\text{C}_1\text{-C}_{10}\text{COR}^2$,
- phenyl optionally substituted with halo, $\text{C}_1\text{-C}_4$ alkyl, or $\text{C}_1\text{-C}_4$ alkoxy,
- tetrazolo;

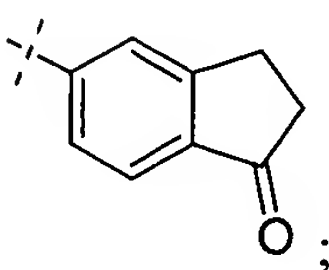
R^7 is

- phenyl or heteroaryl containing 3-6 C and 1-3 O, N, or S atoms, each optionally substituted by $\text{C}_1\text{-C}_4$ alkyl, CN, NO_2 , $\text{CO-C}_1\text{-C}_4\text{alkyl}$, $\text{C}_1\text{-C}_4$ alkoxy, or $\text{C}_1\text{-C}_4$ haloalkyl,
- CO-R^8 ,

•



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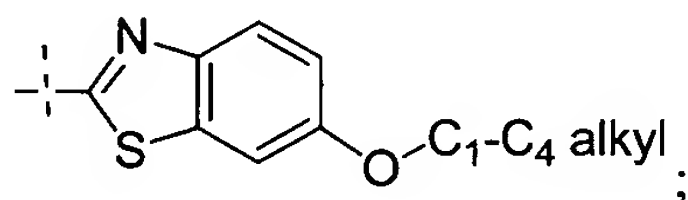


R⁸ is

- C₁-C₆ alkyl optionally substituted with C₁-C₄ alkoxy, N(CH₃)₂, or one or two CF₃,
- C₃-C₆-cycloalkyl,
- phenyl optionally substituted with C₁-C₄ alkoxy, halo, or C₁-C₄ alkyl,
- NH-phenyl optionally substituted with C₁-C₄ alkyl, halo, C₁-C₄ alkoxy, or C₁-C₄ haloalkoxy,
- NH-cyclohexyl;

R⁹ is

- C₃-C₆ cycloalkyl,
- thienyl optionally substituted with C₁-C₄ alkyl or isoxazolyl,
- pyridyl optionally substituted with -SO₂-C₁-C₄alkyl,
- pyrazolyl optionally substituted with halo or C₁-C₄ alkyl,
- isoxazolyl optionally substituted with C₁-C₄ alkyl, or
-



a is 0, 1, 2, 3, 4, or 5;

b is 0, 1, or 2;

d is 1, 2, or 3;

e is 1 or 2;

and pharmaceutically acceptable salts and esters thereof.

2. (Original) The compound of claim 1 wherein Y is

- halo,
- R⁶,
- SR¹,
- S(O)_b-phenyl-CO₂R¹,
- phenyl optionally fused to one or two phenyl rings, or to a 5- or 6-membered heterocycle containing one or more heteroatoms each independently selected from N, S, and O, or

- a 5- or 6-membered heterocycle containing one or more heteroatoms each independently selected from N, S and O, optionally fused to a phenyl ring, each cyclic moiety being optionally substituted with one or more substituents independently selected from

- COR²,
- halo,
- NO₂,
- OR¹,
- R¹,
- SR¹,
- SO₂NR¹R⁷,
- NR¹R¹,
- NR¹COC₁-C₆alkyl,
- C₁-C₁₀COR²,
- phenyl,
- tetrazolo;

and pharmaceutically acceptable salts and esters thereof.

3. (Original) The compound of claim 1 wherein Y is

- phenyl optionally fused to one or two phenyl rings, or to a 5- or 6-membered heterocycle containing one or more heteroatoms each independently selected from N, S, and O, or
- a 5- or 6- membered heterocycle containing one or more heteroatoms each independently selected from N, S and O, optionally fused to a phenyl ring, each cyclic moiety being optionally substituted with one or more substituents independently selected from

- COR²,
- halo,
- NO₂,
- OR¹,
- R¹,
- SR¹,
- SO₂NR¹R⁷,

- NR^1R^1 ,
- $\text{NR}^1\text{COC}_1\text{-C}_6\text{alkyl}$,
- $\text{C}_1\text{-C}_{10}\text{COR}^2$,
- phenyl,
- tetrazolo;

and d is 1 or 2;

and pharmaceutically acceptable salts and esters thereof.

4. (Currently amended) The compound of claim 1 wherein

Y is

- phenyl optionally fused to one or two phenyl rings, or to a 5- or 6-membered heterocycle containing one or more heteroatoms each independently selected from N, S, and O, or
 - a 5- or 6- membered heterocycle containing one or more heteroatoms each independently selected from N, S and O, optionally fused to a phenyl ring,
- each cyclic moiety being optionally substituted with one or more substituents independently selected from

- COR^2 ,
- halo,
- NO_2 ,
- OR^1 ,
- R^1 ,
- SR^1 ,
- $\text{SO}_2\text{NR}^1\text{R}^7$,
- NR^1R^1 ,
- $\text{C}_1\text{-C}_{10}\text{COR}^2$,
- phenyl,
- tetrazolo;

Ar is

- ~~phenyl optionally fused to a 5- or 6-membered heterocycle containing one or more heteroatoms each independently selected from O, S, and N, said bicyclic moiety being optionally fused to a phenyl, or~~

- ~~• a 5- or 6- membered heterocycle containing one or more heteroatoms each independently selected from N, S, and O, optionally fused to phenyl;~~

and d is 1 or 2;

and pharmaceutically acceptable salts and esters thereof.

5. (Currently amended) The compound of claim 1 wherein

Y is

- phenyl optionally fused to one or two phenyl rings, or to a 5- or 6-membered heterocycle containing one or more heteroatoms each independently selected from N, S, and O, or
 - a 5- or 6- membered heterocycle containing one or more heteroatoms each independently selected from N, S and O, optionally fused to a phenyl ring,
- each cyclic moiety being optionally substituted with one or more substituents independently selected from

- COR²,
- halo,
- OR¹,
- R¹,
- NR¹R¹,

Ar is

~~• phenyl or~~

~~• a 5- or 6- membered heterocycle containing one or more N atoms;~~

a is 0, 1, 2, or 3; and

d is 1;

and pharmaceutically acceptable salts and esters thereof.

6. (Currently amended) A compound selected from the group consisting of:

~~2-[4-(ethoxycarbonyl)phenoxy]-4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]benzoic acid;~~

~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-2-isobutylbenzoic acid;~~

~~N-{3-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-~~

~~-chromen-6-yl]benzoyl}-2-methylbenzenesulfonamide;~~
~~4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-2-isobutoxybenzoic acid;~~
~~N-{3-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzoyl}-4-methoxybenzenesulfonamide;~~
~~N-{3-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzoyl}-1-propanesulfonamide;~~
~~4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-N-(4-methoxybenzoyl)benzenesulfonamide;~~
~~N-(2-cyano-4-nitrophenyl)-3-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzenesulfonamide;~~
~~2-(4-chlorophenoxy)-4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzoic acid;~~
~~N-(4,6-dimethoxy-2-pyrimidinyl)-4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-2-(trifluoromethoxy)benzenesulfonamide;~~
~~2-(4-fluorophenoxy)-4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzoic acid;~~
~~4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-N-(3-methoxybenzoyl)benzenesulfonamide;~~
~~4-fluoro-N-{3-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzoyl}benzenesulfonamide;~~
~~4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-2-(4-methylphenoxy)benzoic acid;~~
~~4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-2-(2-phenylethyl)benzoic acid;~~
~~3-chloro-4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzoic acid;~~
~~N-(4-fluorobenzoyl)-4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzenesulfonamide;~~
~~4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-3-methoxybenzoic acid;~~
~~4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-2-phenoxybenzoic acid;~~

~~N-(4-cyanophenyl)-4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-2-(trifluoromethoxy)benzenesulfonamide;~~
~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-N-(4-methoxy-6-methyl-2-pyrimidinyl)-2-(trifluoromethoxy)benzenesulfonamide;~~
~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-N-(3,3,3-trifluoropropanoyl)benzenesulfonamide;~~
~~2-hydroxy-4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]benzoic acid;~~
~~3-((1R)-2-(((2R)-6-{4-[(4-fluorophenyl)amino]carbonyl}amino)sulfonyl]phenyl)-3,4-dihydro-2H-chromen-2-yl)methyl]amino)-1-hydroxyethyl)pyridine;~~
~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-N-(2-pyrimidinyl)benzenesulfonamide;~~
~~N-benzoyl-4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]benzenesulfonamide;~~
~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-2-propoxybenzoic acid;~~
~~N-({4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-2-pyridinyl}carbonyl)-4-methoxybenzenesulfonamide;~~
~~3-((1R)-1-hydroxy-2-(((2R)-6-{4-[(4-methylphenyl)amino]carbonyl}amino)sulfonyl]phenyl)-3,4-dihydro-2H-chromen-2-yl)methyl]amino)ethyl)pyridine;~~
~~3-((1R)-2-(((2R)-6-{4-[(4-chloro-2-methylphenyl)amino]carbonyl}amino)sulfonyl]phenyl)-3,4-dihydro-2H-chromen-2-yl)methyl]amino)-1-hydroxyethyl)pyridine;~~
~~N-(ethoxyacetyl)-4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]benzenesulfonamide;~~
~~N-(3,3-dimethylbutanoyl)-4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]benzenesulfonamide;~~
~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide;~~
~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-2-[4-(methylsulfonyl)phenoxy]benzoic acid;~~
~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-3-methylbenzoic acid;~~
~~4-{2-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl]-3,4-dihydro-2H-chromen-6-yl}ethyl]benzoic acid;~~

~~N-(2,2-dimethylpropanoyl)-4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzenesulfonamide;~~

~~3-[(1R)-2-([(2R)-6-(4-[(anilinocarbonyl)amino]sulfonyl)phenyl)-3,4-dihydro-2H-chromen-2-yl)methyl]amino)-1-hydroxyethyl]pyridine;~~

~~2-ethoxy-4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzoic acid;~~

~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-N-(4-methoxy-6-methyl-2-pyrimidinyl)benzenesulfonamide;~~

~~3-[(1R)-2-([(2R)-6-[4-[(cyclohexylamino)carbonyl]amino]sulfonyl)phenyl]-3,4-dihydro-2H-chromen-2-yl)methyl]amino)-1-hydroxyethyl]pyridine;~~

~~N-(cyclopropylcarbonyl)-4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzenesulfonamide;~~

~~2-chloro-5-fluoro-4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzoic acid;~~

~~4-[(4-[R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzoic acid;~~

~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-2-methylbenzoic acid;~~

~~2-fluoro-4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzoic acid;~~

~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-3-propoxybenzoic acid;~~

~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-2-isopropoxybenzoic acid;~~

~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-N-(1,3-thiazol-2-yl)benzenesulfonamide;~~

~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-2-(4-methoxyphenoxy)benzoic acid;~~

~~3-(cyclopropylmethoxy)-4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzoic acid;~~

~~4-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]benzenesulfonamide;~~

~~5-[(2R)-2-([(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino)methyl)-3,4-dihydro-2H-chromen-6-yl]-4'-methyl-1,1'-biphenyl-2-carboxylic acid;~~

~~N-{6-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-3-pyridinyl}benzenesulfonamide;~~
~~4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-N-(3-pyridinyl)benzenesulfonamide;~~
~~4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-2-methoxybenzoic acid;~~
~~4-chloro-N-{6-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-3-pyridinyl}benzenesulfonamide;~~
~~4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-3-isobutoxybenzoic acid;~~
~~N-{6-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-3-pyridinyl}methanesulfonamide;~~
~~3-{2-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl}ethyl}benzoic acid;~~
~~3-[(1E)-1-hexenyl]-4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl}benzoic acid;~~
~~3-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-N-(2-pyrimidinyl)benzenesulfonamide;~~
~~4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-2-(2-methoxyethoxy)benzoic acid;~~
~~4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl]-2,6-dimethylbenzoic acid;~~
~~4-[(2R)-2-(((2R)-2-(6-amino-3-pyridinyl)-2-hydroxyethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl}benzoic acid;~~
~~3-[(2R)-2-(((2R)-2-(6-amino-3-pyridinyl)-2-hydroxyethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl}benzoic acid;~~
~~(1R)-1-(6-amino-3-pyridinyl)-2-(((2R)-6-[4-(1H-tetrazol-5-yl)phenyl]-3,4-dihydro-2H-chromen-2-yl)methyl)amino}ethanol;~~
~~5-{4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl}phenyl}-3-phenyl-1,2,15,3,15,4-thiatriazole-2-carboxylic acid;~~
~~5-{4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl}phenyl}-2-furoic acid;~~
~~5-{4-[(2R)-2-(((2R)-2-hydroxy-2-(3-pyridinyl)ethyl)amino)methyl]-3,4-dihydro-2H-chromen-6-yl}phenyl}-2-thiophenecarboxylic acid;~~

~~5-{4-[(2R)-2-({[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino}methyl)-3,4-dihydro-2H-chromen-6-yl]phenyl}-3-thiophenecarboxylic acid;~~
~~4-{4-[(2R)-2-({[(2R)-2-hydroxy-2-(3-pyridinyl)ethyl]amino}methyl)-3,4-dihydro-2H-chromen-6-yl]phenyl}-2-thiophenecarboxylic acid;~~
~~6-[(2R)-2-({[(2R)-2-(6-amino-3-pyridinyl)-2-hydroxyethyl]amino}methyl)-3,4-dihydro-2H-chromen-6-yl]nicotinic acid;~~
~~5-[(2R)-2-({[(2R)-2-(6-amino-3-pyridinyl)-2-hydroxyethyl]amino}methyl)-3,4-dihydro-2H-chromen-6-yl]nicotinic acid;~~
~~2-[(2R)-2-({[(2R)-2-(6-amino-3-pyridinyl)-2-hydroxyethyl]amino}methyl)-3,4-dihydro-2H-chromen-6-yl]-4-pyridinecarboxylic acid;~~
~~1-({[(2R)-2-({[(2R)-2-(6-amino-3-pyridinyl)-2-hydroxyethyl]amino}methyl)-3,4-dihydro-2H-chromen-6-yl]carbonyl]amino)cyclopropanecarboxylic acid; and~~
~~4-[(2R)-2-({[(2R)-2-(3-chlorophenyl)-2-hydroxyethyl]amino}methyl)-3,4-dihydro-2H-chromen-6-yl]benzoic acid (Example 344).~~

7. (Cancelled).
8. (Original) A method of treating obesity comprising the step of administering to a patient in need thereof a pharmaceutically effective amount of a compound of claim 1.
9. (Original) A method of treating diabetes comprising the step of administering to a patient in need thereof a pharmaceutically effective amount of a compound of claim 1.
10. (Original) A method of treating a patient with impaired fasting glucose or impaired glucose tolerance comprising the step of administering to said patient in need thereof a pharmaceutically effective amount of a compound of claim 1.
11. (Original) A method of treating gastrointestinal disorders comprising the step of administering to a patient in need thereof a pharmaceutically effective amount of a compound of claim 1.
12. (Original) A method of treating hypertriglyceridemia, hypercholesterolemia, atherosclerotic disorders, or cardiovascular disorders comprising the step of administering to a patient in need thereof a pharmaceutically effective amount of a compound of claim 1.
13. (Original) A method for lowering high-density lipoprotein levels comprising the step of administering to a patient in need thereof a pharmaceutically effective amount of a compound of